

**REMARKS**

**STATUS OF THE APPLICATION**

With this amendment, claims 1, 3, 5, 8-14, 20, 23, and 27 have been amended, claims 18-19, 24-26, and 28-29 have been canceled, and new claims 30-32 have been added. Thus, claims 1-17, 20-23, 27, and 30-32 are currently pending. No new matter has been added with these claim amendments.

**CLAIM REJECTIONS – 35 U.S.C. §101**

Claims 24-26 are rejected under 35 U.S.C. §101. The Examiner states in the March 24, 2008 office action that, “the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35. U.S.C. 101”. Applicants have canceled claims 24-26 and submit that the rejection with respect to these claims is now moot.

**CLAIM REJECTIONS – 35 U.S.C. §112, SECOND PARAGRAPH**

Claims 1-20 and 23-29 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner states in the March 24, 2008 office action that, the “Nature of Q and Ar rings is not completely defined as only 2 atoms are positively recited as ring members” and that, “the nature of the remaining ring atoms is not clear”. Applicants have amended claims 1 and 3 to delete the language, “which possesses 1 or 2 N atoms as ring members” in connection with the Q and Ar definitions. Thus, Applicants submit that this rejection is overcome.

The Examiner states in the office action that the language, ““where appropriate...’ appearing throughout the dependent claims is not clear as to what conditions the functional groups following this term can be present and when it is not appropriate”. In claims 10, 11, and 23, Applicants have deleted the language “where appropriate”. Thus, Applicants submit that this rejection is overcome.

The Examiner states in the office action that, "In claims 12 and 20 the wording 'R<sup>1</sup> is different from hydrogen and methyl' is grammatically awkward". Applicants have amended claims 12 and 20 to replace the language, "R<sup>1</sup> is different from hydrogen and methyl" with the language, "R<sup>1</sup> is not hydrogen or methyl". Thus, Applicants submit that this rejection is overcome.

In the office action the Examiner states that, "Method claim 27 is of indeterminate scope as no particular disorder is ever recited". Applicants have amended claim 27 to include the language that the medical disorder is "selected from Parkinson's disease and schizophrenia". Thus, Applicants submit that this rejection is overcome.

In the office action the Examiner states that, "Claims 24-26 provide for the use of compounds, but since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass". Applicants have canceled claims 24-26, and Applicants submit that the rejection of these claims is now moot.

In the office action, the Examiner states that there is extraneous text in claim 1 (See "Ar" definition, 5<sup>th</sup> line) and in claim 3 (See "Ar" definition, 4<sup>th</sup> line). Applicants have deleted the extraneous text from claims 1 and 3, and Applicants submit that this rejection is overcome.

#### **CLAIM REJECTIONS – 35 U.S.C. §112, FIRST PARAGRAPH**

Claims 26-28 are rejected under 35 U.S.C. §112, first paragraph. The Examiner states in the office that, "the specification, while being enabling for treating schizophrenia and Parkinson's Disease, does not reasonably provide enablement for treating any CNS disorder or kidney disorder". Applicants have canceled claims 26 and 28, and Applicants submit that the rejection of these claims is now moot. Applicants have amended claim 27 so that the medical disorder is "selected from Parkinson's disease and schizophrenia." Thus, Applicants submit the rejection of claim 27 is overcome.

#### **Enablement**

Claims 1-29 are rejected under 35 U.S.C. §112, first paragraph. The Examiner states in the office action that, "the specification, while being enabling for Q as pyridyl, pyrimidyl and Ar as phenyl and R2 as alkyl, does not reasonably provide enablement for the varying scope of azines permitted at both Q and Ar as well as fused piperazines at R1/R2 and at any pair of R2".

Applicants have canceled claims 18-19, 24-26, and 28-29, and Applicants submit that the rejection of these claims is now moot. Applicants respectfully traverse the Examiner's rejection of the remaining claims. Applicants have amended the claims so that, "Q is a bivalent, 6-membered heteroaromatic radical selected from pyridiyl and pyrimidiyl" and "Ar is phenyl or a 6-membered heteroaromatic radical selected from pyridyl and pyrimidyl". Thus, Applicants submit that with these claim amendments, this rejection is overcome.

The Examiner further states that, "The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims," and that, "There is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and no exemplary test data has been provided for such a scope." Applicants submit and attach hereto as Exhibit 1, a Declaration under 37 C.F.R. §1.132 of inventor Wilfried M. Braje. In the Declaration, the synthesis and the biological test data of further compounds which fall under the scope of claim 1 are presented. This data provides, for example, support for compounds, wherein R<sup>1</sup> and R<sup>2</sup> together form an alkylene group; for compounds, wherein two residues R<sup>2</sup> together form an alkylene group; for compounds, wherein R<sup>a</sup> is NR<sup>b</sup>R<sup>c</sup>, CN or halogen; and for compounds, wherein R<sup>b</sup> is haloalkoxy. In support of the argument that the subject application is enabling with regard to the synthesis of compounds wherein Ar is a heterocyclic residue, Applicants submit and attach hereto as Exhibit 2, results of an internet search ([www.emolecules.com](http://www.emolecules.com)), where it can be seen that pyridyl sulfonyl chlorides and pyrimidyl sulfonyl chlorides having various kinds of substituents which fall under the scope of claim 1 are commercially available. These sulfonyl chlorides can be used in the general method for the preparation of compounds I which is described in the subject application.

Applicants further submit and attach hereto as Exhibit 3, the results of a search (SciFinder and ACDFinder) where it can be seen that bridged and condensed piprazines which can be used in the general method for the preparation of compounds of formula I described in the subject application are also commercially available (see also Exhibit 2 [www.emolecules.com](http://www.emolecules.com)). As to the definition of radicals of the compound of formula I which are not supported by specific examples in the specification or in the enclosed declaration, it has to be noted that most of these radicals are chemically and biologically equivalent to radicals having meanings supported by the

test data. For example, compounds wherein R is NR<sup>3</sup>, wherein R<sup>3</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl, can be expected to have a similar biological effect as compared to the same compounds wherein R is NH. In addition, compounds wherein R<sup>a</sup> is NH<sub>2</sub> or NHR<sup>6</sup> can be expected to have a biological effect comparable to that of compounds wherein R<sup>a</sup> is NR<sup>6</sup>R<sup>7</sup>. Since the positive effect of compounds I with R<sup>a</sup> being C<sub>1</sub>-C<sub>4</sub>-alkyl or halogen has been proven in the test examples, it is clear that the same compound wherein R<sup>a</sup> is C<sub>1</sub>-C<sub>4</sub>-haloalkyl can be expected to have a comparable biological effect since this residue combines the properties of alkyl and halogen. The same considerations apply to varying residues R<sup>b</sup>. Since compounds wherein R<sup>b</sup> is C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-haloalkyl or C<sub>1</sub>-C<sub>6</sub>-haloalkoxy have proven to have the desired biological effect, one skilled in the art can expect the same effect for compounds wherein R<sup>b</sup> is C<sub>1</sub>-C<sub>6</sub>-alkoxy, since this residue combines the properties of alkyl and haloalkoxy. As the test data shows, using a halogenated alkyl residue instead of a halogen-free alkyl residue R<sup>b</sup> apparently has no dramatic effect on the biological activity of the compound. Thus, it can be expected that using a non-halogenated alkoxy substituent instead of a halogenated alkoxy group R<sup>b</sup> will not change the biological activity of the compound. The same rationale applies to R<sup>b</sup> being C<sub>3</sub>-C<sub>6</sub>-cycloalkyl-C<sub>1</sub>-C<sub>4</sub>-alkyl. Since compounds having C<sub>3</sub>-C<sub>6</sub>-cycloalkyl groups or C<sub>1</sub>-C<sub>4</sub>-alkyl groups have proven to be useful dopamine D<sub>3</sub> ligands, the same can be expected for compounds wherein R<sup>b</sup> is C<sub>3</sub>-C<sub>6</sub>-cycloalky-C<sub>1</sub>-C<sub>4</sub>-alkyl, which represents a combination of the two former named groups. The same applies to compounds wherein R<sup>b</sup> is NHR<sup>6</sup>, since it has been shown that compounds wherein R<sup>b</sup> is NR<sup>6</sup>R<sup>7</sup> show a good biological activity. Finally, since cyano groups and halogen residues are considered to be bioisosters, it can be expected that compounds wherein R<sup>b</sup> is CN also exhibit the desired biological activity.

In view of the attached Declaration and evidence in support of enablement of the subject application, Applicants respectfully request that the enablement rejection be withdrawn.

#### **CLAIM OBJECTIONS – 37 C.F.R. §1.75(c)**

Claims 8 and 19 are objected to under 37 C.F.R. §1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. The Examiner states in the office action that, "Claim 8 permits A<sub>2</sub> as N which is not included within [claim] 6 which [claim] 8 depends". Applicants have amended claim 8 to depend from claim 5, and Applicants submit that the Examiner's objection is overcome. The Examiner further states in the office action that, "In claim 19 phenyl is recited for Ar which is not included in claim 13". Applicants have canceled claim 19, and Applicants submit that the objection is now moot.

**CLAIM REJECTIONS – 35 U.S.C. §102(b) and §102(e)**

Claims 1 and 11 are rejected under 35 U.S.C. §102(b) as being anticipated by Interchim Intermediates (“Interchim”). The Examiner states in the office action that Interchim “depicts a compound named therein which is embraced by the instant claim language” and that, “It appears to be part of a Chemical library used as synthetic reagents”. Applicants respectfully traverse the Examiner’s rejection of the claims. Applicants have amended claim 1 to delete “NH<sub>2</sub>” from the definition of R<sup>b</sup> in the definition of Ar. Thus, Applicants submit that claim 1, as amended, and dependent claim 11 are no longer anticipated by the cited Interchim reference.

Claims 1-3, 10 and 11 are rejected under 35 U.S.C. §102(b) as being anticipated by the Willecomme article (“Willecomme”). The Examiner states in the office action that Willecomme “describes compounds within the instant scope. See Table IV, cgs. VII and IV in the 1<sup>st</sup> row of the reaction scheme”. Applicants respectfully traverse the Examiner’s rejection of the claims. Applicants have amended claim 1 to delete “NH<sub>2</sub>” from the definition of R<sup>b</sup> in the definition of Ar. Thus, Applicants submit that claim 1, as amended, and dependent claims 2-3, 10 and 11 are no longer anticipated by the cited Willecomme reference.

Claims 1-3, 10, 11 and 23 are rejected under 35 U.S.C. §102(e) as being anticipated by WO 2004/058265 to Jones (“Jones”). The Examiner states in the office action that Jones “describes several compounds within the claims’ scope as part of a library used for screening binding at various receptors such as neuropeptides” and “describes compounds within the instant scope when pyrazine is present corresponding to instant Q”. Applicants respectfully traverse the Examiner’s rejection of the claims. Applicants have amended claim 1 to recite that “Q is a bivalent, 6-membered heteroatomic radical selected from pyridindiyil and pyrimidindiyil”. Jones discloses pyrazine moieties that are not encompassed by the claims, as amended. Thus, Applicants submit that claim 1, as amended, and dependent claims 2-3, 10 and 11 are no longer anticipated by the cited Jones reference.

Since all of the elements of Applicants’ claimed invention, as amended, are not disclosed or taught by the cited Interchim, Willecomme or Jones references, Applicants’ claimed invention, as amended, cannot be anticipated by Interchim, Willecomme or Jones. In view of the amendments to the claims, Applicants respectfully request withdrawal of the rejection of the claims under 35 U.S.C. §102(b) and §102(e).

### **CLAIM REJECTIONS – OBVIOUSNESS-TYPE DOUBLE PATENTING**

Claims 1-29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of U.S. Patent No. 7,320,979 to Braje et al., which is commonly owned by Applicants. The Examiner states in the office action that, “Although the conflicting claims are not identical, they are not patentably distinct from each other because they embrace overlapping subject matter to a large degree”, and that, “While having the same inventive entity as herein and disclosure as well, US'979 does not share a common patent with the instant case”. Applicants wish to hold this rejection in abeyance until notification by the Examiner of allowable subject matter. Upon such notification, a terminal disclaimer will be filed.

### **OBJECTION TO IDS**

In the office action the Examiner states that the second page of Applicants’ IDS filed on 10/11/05 contains improper citations, and that although some of the cites have been properly cited in the IDS filed on 9/25/06, the remaining references should be resubmitted in the format set forth in M.P.E.P. §609. Applicants resubmit herewith an IDS with the remaining references in the proper citation format.

### **CONCLUSION**

Claims 1-17, 20-23, 27, and 30-32 are currently pending in the subject application. In view of the claim amendments and remarks set forth above, Applicants submit that the subject application is in condition for allowance and respectfully requests reconsideration and withdrawal of all the claim rejections.

Should the Examiner have any questions or should the Examiner wish to discuss any matters in connection with the subject application, the Examiner is invited to contact the undersigned.

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